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Signed: Barbara Bryant
Barbara Bryant

Dated: July 25, 2007

PATENT

In the United States Patent and Trademark Office

Applicant: Clark et al.
Applicant's Ref: 0037.00
Application No: 09/414,384
Filed: October 7, 1999
Title: FLOW RESISTANCE MODULATED AEROSOLIZED ACTIVE AGENT DELIVERY

Confirmation No.: 3236
Examiner: Annette Fredricka Dixon
Group Art Unit: 3771

APPEAL BRIEF

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the Examiner's Final Rejection of September 11, 2006, the Applicant of the above-referenced patent application (hereinafter Appellant) hereby appeals to the Board of Patent Appeals and Interferences. Appellant requests the reversal of the Final Rejection.

(1) ***Real Party in Interest***

The real party in interest of the present application is Nektar Therapeutics (formerly Inhale Therapeutic Systems, Inc.), having a place of business at 150 Industrial Road; San Carlos, California 94707.

(2) ***Related Appeals and Interferences***

Appellant, Appellant's legal representative, and assignee are aware of no appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the present appeal.

(3) ***Status of Claims***

Claims 21-36 are presently pending in the case. Claims 1-20 have been cancelled. Claims 21-36 have been finally rejected. The rejection of each of claims 21-36 is hereby appealed.

(4) ***Status of Amendments***

No amendments after Final Rejection have been filed. Accordingly, all amendments made during prosecution of the case have been entered.

(5) ***Summary of the Claimed Subject Matter***

The presently claimed invention is directed to methods and devices for delivering an active agent formulation to the lungs of a human patient. The active agent formulation if delivered at a low flow rate initially and then at a higher flow rate.

As discussed on page 10, line 24 through page 11 line 20, the delivery of an aerosolized active agent may be controlled by providing a valve that provides a high flow resistance, such as a flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM, at the onset of the patient's inhalation and that subsequently opens to provide a lower flow resistance. The lower flow resistance allows for a higher flow rate through the device. A chart showing an exemplary flow resistance profile is shown in Figure 3.

It has been discovered that by providing an initially high flow resistance and then a subsequently lower flow resistance, increased bioavailability of the active agent can be achieved.

(6) *Grounds of Rejection to be Reviewed on Appeal*

Appellant requests review of the Examiner's following grounds of rejection:

Claims 21-36 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,655,520 to Howe et al (hereinafter Howe et al).

(7) *Argument*

The Examiner's rejection of claims 21-36 under 35 USC 103(a) as being unpatentable over Howe et al is improper. First, Howe et al does not teach or suggest all features positively set forth in the claims. Secondly, one of ordinary skill in the art at the time the invention was made would not have found it obvious to make the modification to Howe et al proposed by the Examiner. If the Examiner is wrong in either case, the rejection cannot be sustained.

Howe et al does not teach or suggest all elements in Claim 21

Howe et al does not render Applicant's invention as set forth in independent claim 21 unpatentable because it does not teach or suggest all features positively recited in the claim. Claim 21 is to a device for controlling the delivery of an aerosolized active agent to the lungs comprising, inter alia, a valve that provides a high flow resistance at the onset of the patient's inhalation and that subsequently opens to provide a lower flow resistance, wherein the lower flow resistance allows for a higher flow rate through the device. This feature is not present in Howe et al.

Howe et al discloses an aerosolization device with a flow regulator valve (see element 1000 and Figures 3a-3c). The Howe et al flow regulator valve provides a maximum opening, i.e. a minimum flow resistance, when a patient is inhaling weakly and a minimum opening, i.e. a maximum flow resistance, when a patient is inhaling strongly (see column 4 line 65 through column 6 line 10). The flow regulator valve by adjusting its flow resistance allows

for a consistent flow rate to be achieved through the Howe et al device for various patient inhalation strengths. This flow regulator valve of Howe et al *is not* similar to the valve recited in Appellant's claim 21 and is, in fact, quite the opposite thereof. Appellant's valve provides a high flow resistance at the onset of the patient's inhalation when the inhalation strength is at a minimum. This is in contrast to Howe et al's valve which operates oppositely. Appellant's valve also subsequently opens to provide a lower flow resistance than the flow resistance at the onset of inhalation. Again, this is distinctly opposite from the manner of operation of Howe et al's valve in which its minimum flow resistance would occur at the onset of inhalation. Appellant's valve and Howe et al's valve are, simply, not at all related valves. Howe et al is concerned with maintaining a consistent flow rate while Appellant's valve is concerned with providing an altered flow rate. Appellant is concerned with providing little or no flow through the device initially and subsequently providing high flow through the device. Howe et al's valve is not capable of providing such and therefore does not satisfy the claim limitations in Appellant's claim 21.

The Examiner's position that Howe et al's valve meets the limitations of claim 21 is not proper and is a distortion of the teachings of Howe et al. The Examiner states on page 3 of the Final Office Action that "Howe et al. provide a high flow resistance at the onset of a patient's inhalation by closing at least partially (fig. 3b) against an inhalation flow rate..." This, however, does not satisfy the limitations of Appellant's claim 21. Once there is sufficient inhalation to cause a closing of the Howe et al valve, you are no longer "at the onset" of inhalation. Read in its proper light, without the distortion that occurs by stretching the reference out of its proper context, the Howe et al valve and the Appellant's valve are opposites. Howe et al's valve is at a minimum flow resistance at the onset of inhalation and subsequently increases flow resistance during inhalation. The Appellant's valve is at a maximum flow resistance at the onset of inhalation and subsequently decreases flow resistance during inhalation.

In addition, Howe et al does not render claim 21 unpatentable because Howe et al specifically teaches away from Applicant's claimed invention. As recited in claim 21, the lower flow resistance allows for a higher flow rate through the claimed device. This is in direct opposition to the teachings of Howe et al. The purpose of Howe et al is to regulate the flow resistance in order to provide a constant flow rate (see column 2 lines 30-37). Thus, Howe et al does not teach the alteration of flow rate and, in fact, specifically teaches against it. Accordingly, one of ordinary skill in the art would not have found it obvious to alter Howe et al in a manner that would arrive at Applicant's invention since doing so would destroy the purpose of the Howe et al device.

Since Howe et al does not disclose or suggest all positively set forth elements of claim 21, it does not render claim 21 unpatentable. A reversal of the rejection is requested.

Examiner's proposed modifications to Howe et al are not obvious

Even if it was fair and proper to construe Howe et al as the Examiner has done above, Howe et al still does not disclose a valve that has a flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM at the onset of the patient's inhalation, as required by Appellant's claim 21. Accordingly, Howe et al does not render claim 21 unpatentable for this additional reason.

The Examiner's contention that a flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM is "an obvious matter of design choice" is wholly unsupported and is not correct. If one of ordinary skill in the art were to be motivated to alter the Howe et al device, that person would necessarily be motivated to alter the device in a manner that is consistent with the teachings of the Howe et al reference. That is, one of ordinary skill in the art would design a flow regulator valve that maintains a consistent flow through the device as taught by Howe et al and would not be motivated to make an entirely new type of valve that has a very high flow resistance at onset and thereby limits the flow through the device. The Examiner has provided no reasoning behind the proposition that such a modification would be obvious, because it simply would not be. A flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM is exceptionally high and is intended to allow for little or no flow through the device. To provide the Howe et al device with that flow resistance (particularly at the onset of inhalation) would render the Howe et al device inoperative for a significant portion of the population of patients.

Since it would not have been obvious to modify Howe et al to provide the flow resistance required by claim 21, Howe et al does not render claim 21 unpatentable for this additional reason. Therefore, Appellant requests reversal of the rejection of this claim.

Independent claim 28 is also not unpatentable over Howe et al

Claim 28 is also not rendered unpatentable by Howe et al. Claim 28 recites a valve that provides a high flow resistance at the onset of the patient's inhalation and that subsequently opens to provide a lower flow resistance which corresponds to a higher flow rate. Since Howe et al does not disclose a valve which provides a high flow resistance at the onset of

inhalation and which subsequently opens to provide a higher flow rate, as discussed above, Howe et al does not render claim 28 unpatentable.

Claim 28 is also not rendered unpatentable by Howe et al because Howe et al does not disclose additional features recited in the claim. Claim 28 also recites that the valve provides a high flow resistance at the onset of the patient's inhalation and which corresponds to a flow rate of about 15 liters per minute or less and that subsequently opens to provide a lower flow resistance which corresponds to a higher flow rate. Howe et al does not disclose the flow rate that is claimed.

The Examiner's contention on page 4 of the Final Office Action that Howe et al discloses a high flow resistance that results in a flow rate of 15 liters per minute is completely without explicit support within Howe et al or logical support without.

Since Howe et al does not render independent claim 28 unpatentable, Appellant requests the reversal of the Examiner's rejection thereof.

Independent claim 32 is not rendered unpatentble by Howe et al either

Claim 32 is also not rendered unpatentable by Howe et al. Claim 32 recites a valve that is adapted to provide a first flow resistance at the onset of the patient's inhalation and that subsequently opens to provide a second flow resistance, the second flow resistance being less than the first flow resistance. This limitation goes precisely against the express intention of the Howe et al valve, as discussed above. Since Howe et al does not disclose, teach or suggest this feature and since it would not be obvious to go against the express teachings of the reference, Howe et al does not render claim 32 unpatentable. Appellant requests reversal of this rejection, too.

The dependent claims are also allowable

Claims 22-27, 29-31, and 33-36 depend from allowable claims 21, 28 and 32. Accordingly, claims 22-27, 29-31, and 33-36 are also allowable over Howe et al. Reversal of all rejections is hereby requested.

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Conclusion

For the reasons given above, it is believed that all rejections made by the Examiner have been addressed and overcome. Therefore, all pending claims are allowable. A reversal is respectfully requested.

Should there be any questions, Appellant's representative may be reached at the number listed below.

Respectfully submitted,

NEKTAR THERAPEUTICS
(formerly INHALE THERAPEUTIC SYSTEMS)

Dated: 25 July 2007

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(8) Claims Appendix

21. A device for controlling the delivery of an aerosolized active agent to the lungs of a human patient, said device comprising a valve that provides a high flow resistance of at least 0.4 (cm $H_2O)^{½}$ / SLM at the onset of the patient's inhalation and that subsequently opens to provide a lower flow resistance, wherein the lower flow resistance allows for a higher flow rate through the device.

22. A device according to claim 21 wherein the high flow resistance is a resistance of between 0.4 and 2 (cm $H_2O)^{½}$ / SLM.

23. The device of claim 21 wherein the lower flow resistance is a resistance between 0 and 0.3 (cm $H_2O)^{½}$ / SLM.

24. The device of claim 21 wherein the high flow resistance corresponds to a flow rate of 15 liters per minute or less.

25. The device of claim 21 wherein the lower flow resistance corresponds to a flow rate of 15-80 liters per minute.

26. The device of claim 21 wherein the high flow resistance is provided for an initial time period of less than 10 seconds.

27. The device of claim 21 wherein the high flow resistance is provided for an initial time period of less than 5 seconds.

28. A device for controlling the delivery of an aerosolized active agent to the lungs of a human patient, said device comprising a valve that provides a high flow resistance at the onset of the patient's inhalation and which corresponds to a flow rate of about 15 liters per minute or less and that subsequently opens to provide a lower flow resistance which corresponds to a higher flow rate.

29. The device of claim 28 wherein the lower flow resistance corresponds to a flow rate of between about 15 and 80 liters per minute.

30. The device of claim 28 wherein the high flow resistance is a resistance of between about 0.4 and 2 (cm $H_2O)^{½}$ / SLM.

31. The device of claim 28 wherein the high flow resistance is provided for an initial time period of less than about 10 seconds.

32. A device for controlling the delivery of an aerosolized active agent to the lungs of a human patient, said device comprising a valve that is adapted to provide a first flow resistance at the onset of the patient's inhalation and that subsequently opens to provide a second flow resistance, the second flow resistance being less than the first flow resistance, wherein the second flow resistance allows for a higher flow rate.

33. The device of claim 32 wherein the first flow rate is provided for an initial time period of less than about 10 seconds.

34. The device of claim 32 wherein the first flow rate is less than about 15 liters per minute.

35. The device of claim 34 wherein the second flow rate is between about 15 and 80 liters per minute.

36. The device of claim 32 wherein the first flow resistance provides a first flow rate and wherein the second flow resistance provides a second flow rate.

(9) Evidence Appendix

none

(10) Related Proceedings Appendix

none